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HTLV-1 Unrelated Adult T-Cell Leukemia/Lymphoma With Unique Phenotype and Karyotype

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We describe a unique case of adult T-cell leukemia/lymphoma (ATL). The patient had typical clinicohematological features as ATL, but showed a lack of antibody to human T-cell leukemia virus type-1 (HTLV-1) and was negative for HTLV-I proviral DNA in the peripheral mononuclear cells by means of polymerase chain reaction. The phenotype of tumor cells revealed CD7+, CD5+, CD2+, CD3+, WT31−, TcR δ 1−, CD4−, CD8−, CD25−, and the karyotype showed a 5q-, t(12;18). HTLV-I unrelated ATL is very rare, and the karyotype as in our case has not been reported previously. Am. J. Hematol. 64:64–66, 2000.

Key words: HTLV-1; ATL; CD7; CD25; 5q-; t(12;18)

INTRODUCTION

Adult T-cell leukemia/lymphoma (ATL) is a distinct T-cell lymphoproliferative disorder associated with human T-cell leukemia virus type 1 (HTLV-1) [1]. However, the existence of HTLV-1 unrelated ATL clinicohematologically indistinguishable from typical ATL associated with HTLV-1 suggests that factors other than HTLV-1 may be involved in the development of ATL [2]. The authors report a case of HTLV-1 negative ATL with previously unknown karyotype.

CASE REPORT

A 69-year-old man was admitted to Yamada Red Cross Hospital in March, 1995, because of persistent low grade fever. He was born in Ise, Mie (southwest Japan). Physical examination on admission revealed left inguinal lymphadenopathy, hepatosplenomegaly, and reddish skin eruptions on the body. Bone X-rays showed the absence of osteolytic bone lesions. A computed tomography of the abdomen disclosed lymphadenopathy on the para-aortic region. Skin biopsy showed dense aggregates of abnormal lymphocytes in the dermis and epidermis. Hematological data revealed a white blood cell count of 73,500/μL with 45.6% abnormal lymphoid cells with irregular nuclei (Figs. 1 and 2). No abnormal cells were found in a bone marrow specimen. The serum lactate dehydrogenase level was slightly increased to 333 IU/L. Hypercalcemia was not recognized. A serological test for antibodies to HTLV-1 was negative, which was

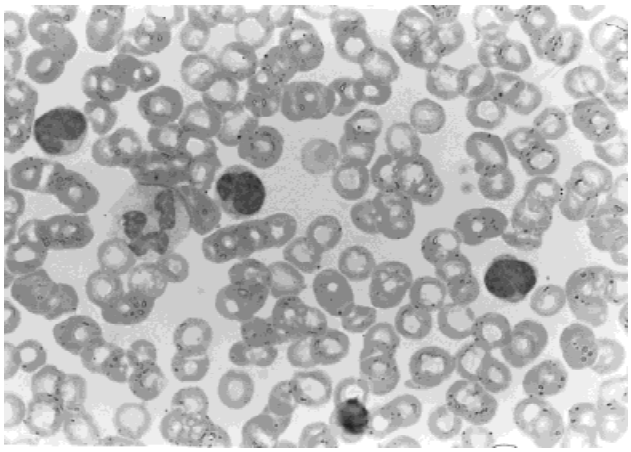

Fig. 1. Peripheral blood film (×1,000, May–Giemsa stain).

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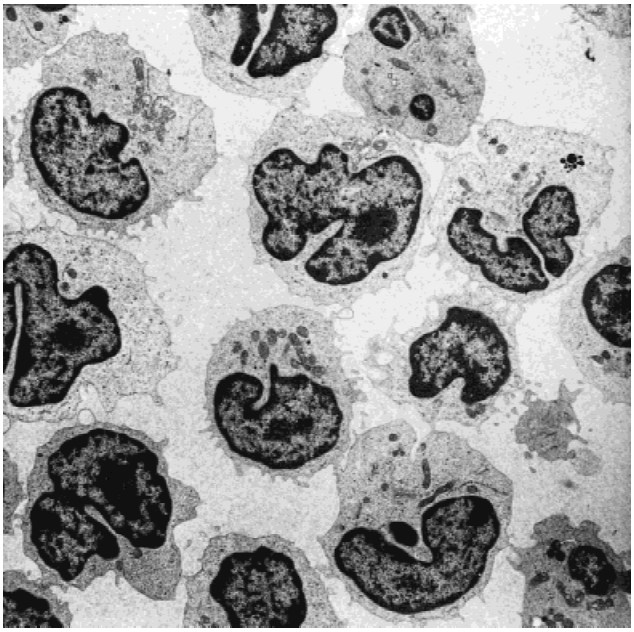

Fig. 2. Electron photomicrograph of abnormal lymphoid cells with irregular nuclei (×3,000).

confirmed by Western blot analysis. The serum level of soluble interleukin-2 receptor (IL-2R) was elevated to over 3000 U/mL. Southern blot analyses showed monoclonal rearrangements of T-cell receptor β and γ genes and germ line configuration of T-cell receptor δ and immunoglobulin heavy chain gene. HTLV-1 proviral DNA was not detected in the peripheral blood (PB) mononuclear cells (MNC) DNA by the polymerase chain reaction (PCR) method. A probe for HTLV-1 DNA used was a 8.25 kb fragment of λ 23-3 [3]. Surface marker analysis of PB MNC using indirect immunofluorescence showed CD2 (T11), 93%; CD3 (Leu4), 82%; CD4 (Leu3a), 6%; CD5 (Leu1), 79%; CD7 (Tp40), 70%; CD8 (Leu2), 6%; WT31 (for T-cell receptor [TcR] αβ), 7%; TcR δ 1 (TcR γ δ), 10%; CD56 (NKH1), 17%; CD10 (J5), 2%; CD19 (Leu12), 3%; CD20 (Leu16), 5%; CD11b (OKM1), 33%; CD13 (MCS2), 6%; CD33 (My9), 5%; HLA-DR (OKIa1), 67%, and CD25 (Tac), 3%. Cytogenetic analysis disclosed a 46, XY, del(5)(q22q31), t(12;18)(p11.2;q21.3), 15s+ in all of 20 metaphases examined by Giemsa-banding technique (Fig. 3). We diagnosed him as a putative HTLV-1 unrelated ATL and treated with a combination chemotherapy consisting of cyclophosphamide, daunorubicin, vincristine, vindesine, etoposide, renimustine, and mitoxantrone. He entered a partial remission transiently; however, soon thereafter the disease progressed and become refractory to various chemotherapy. He died of sepsis in June, 1996.

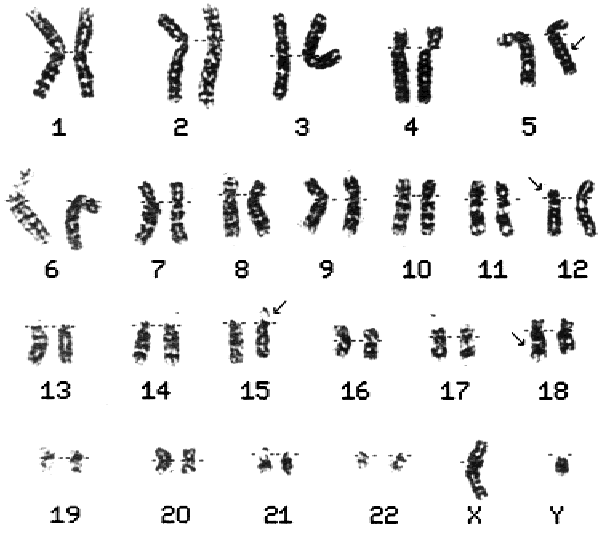

Fig. 3. G-banding karyotype of a leukemic cell of this patient: 46, XY, del(5)(q22q31), t (12;18)(p11.2;q21.3), 15s+.

DISCUSSION

We described here a unique case of ATL not associated with HTLV-1. The patient had clinicohematological findings indistinguishable from typical ATL such as systemic lymphadenopathy, hepatosplenomegaly, skin eruption, abnormal lymphoid cells with irregular nuclei in the peripheral blood, refractory to chemotherapy, and a short clinical course. However, antibodies to HTLV-1 were negative and HTLV-1 proviral DNA could not be detected by means of the PCR method. Though ATL has been shown to be endemic in some regions of the world, especially in southwest Japan, the Caribbean basin and central Africa [1,4,5], HTLV-1 unrelated ATL is very rare, and only several cases have been reported in Japan and Brazil [2,6]. Shimoyama et al. [7] reported three cases and described that there were no detectable differences between the immunologic and karyotype features of HTLV-1 positive and HTLV-1 negative ATLs. This case showed an unusual phenotype (CD7+, CD4−, CD25−) as ATL [8]. In addition, karyotype of our case showing a del(5)(q22), t(12;18)(p11;q21) abnormality was reported previously in neither HTLV-1 positive nor HTLV-1 negative ATL [9]. Since genes for various growth factors and growth factor receptors are located in 5q region [10] and bcl-2 oncogene is associated with 18q21 translocation [11], karyotype abnormality may be related to the development of ATL in our case. Further accumulation of HTLV-1 unrelated ATL and detailed investigation into such cases are needed to truly understand the leukemogenesis of so called ATL.

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